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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,361	09/22/2003	Denis M. Boyle	6794A-000009/US/CPA	4467
30593	7590	07/12/2006	EXAMINER	
HARNESS, DICKEY & PIERCE, P.L.C. P.O. BOX 8910 RESTON, VA 20195			DESAI, ANAND U	
			ART UNIT	PAPER NUMBER
				1653

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/665,361	BOYLE ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Anand U. Desai, Ph.D.	1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 04 May 2005.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-5,8,12,15-17,20,23,26,31,34,37,40,43,51,54 and 205-217 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-5,8,12,15-17,20,23,26,31,34,37,40,43,51,54 and 205-217 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                     | Paper No(s)/Mail Date. _____ .  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|  | 6) <input type="checkbox"/> Other: _____ .                                  |

## **DETAILED ACTION**

1. This office action is in response to Amendment filed on May 4, 2006. New claims 205-217 have been added. Claims 1-5, 8, 12, 15-17, 20, 23, 26, 31, 34, 37, 40, 43, 51, 54, and 205-217 are currently pending and are under examination.

### **Withdrawal of Rejections**

2. The rejection of claims 2, 12, 15, 16, 20, 26, 43, 51, and 54 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

3. The rejection of claims 1, 2, 8, 15, 31, and 37 under 35 U.S.C. 102(b) as being anticipated by Bona et al. (U.S. Patent 5,969,109) is withdrawn.

4. The rejection of claims 1, 2, 8, 15, 31, 37, and 54 under 35 U.S.C. 102(e) as being anticipated by Papadimitriou (U.S. 2002/0037841 A1) is withdrawn.

5. The rejection of claims 1-5, 8, 12, 15, 31, 37, 40, and 54 under 35 U.S.C. 102(e) as being anticipated by Finn et al. (U.S. 2003/0171285 A1; Effective filing date = November 20, 2001) is withdrawn.

### ***Oath/Declaration***

6. A new oath or declaration is required because it is not apparent that the pending application is a Continuation-In-Part of non-provisional U.S. Application Interim Serial No. P-107,891. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly

identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

**Response to Remarks**

7. The examiner acknowledges that the applicants have stated that a new Oath or Declaration will be provided in due time.

**Pending Objections and Rejections**

***Specification***

8. The disclosure is objected to because of the following informalities:
9. There is a typographical error in the amendment to the first sentence describing the corresponding provisional application, “60/412; 227” should be “60/412,227”.
10. There appears to be a typographical error when identifying the filing date of U.S. Application Serial No. 10/662,884. The filing date of record is 9/16/2003.
11. In example 1, at Paragraph [0457], the specification identifies, U.S. application interim serial no. P-107,891 rather than U.S. Serial Number 10/662,884, which was filed on 9/16/2003. Suggest amending to identify U.S. Serial Number 10/662,884, filed September 16, 2003.

***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-5, 8, 12, 15-17, 20, 23, 26, 31, 34, 37, 40, 43, 51, 54, and 205-217 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olson et al. (Chapter 12. Preparation and Characterization of Poly(ethylene glycol)ylated Human Growth Hormone Antagonist: (1997)) in view of Pharmacia Fine Chemicals (Chapter 2. Ion Exchange Chromatography Principles and Methods. Pharmacia Fine Chemicals: (1980)).

Olson et al. describes the pegylation of Growth Hormone Antagonist (GHA) with succinimidyl ester of carboxymethylated methoxy-PEG or the succinimidyl ester of propionic acid of methoxy-PEG. Approximately an equal molar amount of PEG5000 reagent for each potential reactive site was found to be optimal. A protein concentration of 10 mg/ml was used in 50 mM sodium phosphate, pH 7.5. The components were mixed and incubated at room temperature for approximately one hour. Olson et al. describes the use of Phenyl Toyopearl 650M as a hydrophobic interaction chromatography step. The preparation was loaded at a protein concentration of up to 3.7 grams per liter of resin. The main protein peak was pooled and desalted by either G-25 Sephadex or by diafiltration (see pages 171-173, Experimental, PEG Derivatization, and Column Chromatography sections). Olson et al. describes the optimization

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of obtaining a PEGylated GHA with a mass of primarily 40-50 kilodaltons using cation-exchange chromatography. Olson et al. further states "With increasing PEGylation of a protein, there is a reduction in the number of primary amino groups, resulting in decreased ionic interaction with the cationic-exchange resin. Fractions were collected and analyzed by SDS-PAGE...Proteins of higher molecular weight, i.e., containing more PEGylated sites, elute first from the column consistent with their reduced basicity and decreased affinity for the cation-exchange column. This method can be scaled to prepare large quantities of PEGylated proteins with a specific molecular mass range." (see page 174, Results and Discussion, Preparation of PEGylated Proteins section).

The Pharmacia chapter describes the theory of ion exchange. The chapter states "...separation is obtained since different substances have different affinities for the ion exchanger due to differences in their charge. These affinities can be controlled by varying conditions such as ionic strength and pH...In ion exchange chromatography one can choose whether to bind the substance of interest, or to absorb out contaminants and allow the substance of interest to pass through the column" (see section 2.4, The theory of ion exchange, 1<sup>st</sup>, and 2<sup>nd</sup> paragraphs). The chapter also states substances that "...carry both positively and negatively charged groups...are termed amphoteric and the charge that they carry is dependent on pH. At a certain pH value the substance will have zero net charge. This value is termed the isoelectric point (pI) and at this point substances are not bound to any type of ion exchanger. The choice of pH of the starting buffer thus determines the charge on amphoteric samples during the experiment. In principle, therefore, one could use either an anion or a cation exchanger to bind

amphoteric samples by selecting the appropriate pH" (see page 29, section 7.1 Choice of ion exchanger matrix).

One of ordinary skill in the art would have expected to succeed in altering the ionic charge on pegylated GHA, because Olson et al. describes the alteration of ionic association with a cationic-exchange resin due to a reduction in the number of primary amino groups due to pegylation. Furthermore, it would have been obvious to one of skill in the art to alter the ionic association resin by adjusting the pH of the buffer thereby affecting the net charge of PEGylated GHA and favoring the ability to bind an anion exchange resin.

Therefore it would have been obvious to the person having ordinary skill in the art to fractionate the PEGylated GHA using an anion exchange chromatography resin in place of the cation exchange resin described by Olson et al. by adjusting to the appropriate pH as suggested by techniques known in the art as discussed by the Pharmacia chapter (current application, claims 1-5, 8, 12, 15-17, 20, 23, 26, 31, 34, 37, 40, 43, 51, 54, and 205-217).

### *Conclusion*

15. No claims are allowed.
16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

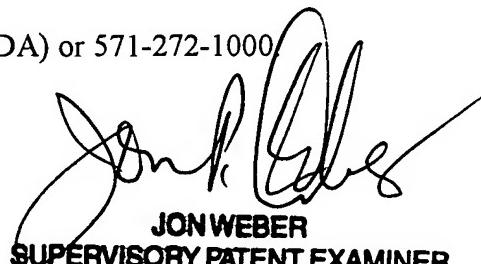
will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

July 6, 2006  


  
JON WEBER  
SUPERVISORY PATENT EXAMINER